I hereby certify that this correspondence is being sent by facsimile transmission (703-872-9306) in accordance with § 1.6(d) addressed to Mail Stop Amendment, Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450, on the date shown

November 10, 2004

PATENT

Docket No. GC 541-3-D1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| In re Application of |) |
|--|-----------------------------|
| Maier et al. |) Group Art Unit: 1623 |
| Serial No.: 10/062,970 |) Examiner: Maier, Leigh C. |
| Filed: February 1, 2002 |) |
| For: Chemically Modified Proteins with |)) |

Supplemental Information Disclosure Statement

Mail Stop Amendment Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Sir:

Applicants are responding to a request by Examiner Maier in a Office Action dated March 25, 2004. Applicants filed a response to the Office Action stating there would be a delay to the Information Disclosure request. Examiner Maier requested that the complete Information Disclosure be resubmitted because the examiner was unable to locate the references submitted for the parent, U.S.S.N. 09/347,029 filed July 2, 1999.

Applicants submit herewith patents, publications or other information (listed on the attached Form PTO-1449 and attached thereto) of which they are aware, that they believe may be material to the examination of this application and in respect of which there may be a duty to disclose in accordance with 37 CFR §1.56.

Those patent(s) or publication(s) which are marked with an asterisk (*) on the attached Form PTO-1449 are not supplied because they were previously signed off by the Examiner.

Serial No. 10/062,970 Page 2

While the information and references disclosed in this Information Disclosure Statement may be "material" pursuant to 37 CFR §1.56, it is not intended to constitute an admission that any patent, publication or other information referred to therein is "prior art" for this invention unless specifically designated as such.

In accordance with 37 CFR §1.97(b), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 CFR §1.56(a) exists. It is submitted that the Information Disclosure Statement is in compliance with 37 CFR §1.98 and MPEP §609 and the Examiner is respectfully requested to consider the listed references.

Respectfully submitted,

Date: November 10, 2004

H. Thomas Anderton, Jr. Registration No. 40,895

Genencor International, Inc. 925 Page Mill Road Palo Alto, CA 94304-1013

Tel: 650 846-7544 Fax: 650 845-6504

U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

NOV 1 2 2004

STATEMENT BY APPLICANT
(Use several sheets if necessary)

ATTY. DOCKET NO.

GC541-3-D1

Previously 23623-7076

SERIAL NO.

10/062,970

APPLICANT Jones et al.

FILING DATE February 1, 2002 GROUP ART UNIT

1623

REFERENCE DESIGNATION U.S. PATENT DOCUMENTS

| EXAM'R INITIAL | | DOCUMENT NUMBER | DATE | NAME | Class | Subclass | Filing Date If Appropriate |
|-------------------|----|--------------------|----------|---------------------|-------|----------|----------------------------|
| | A1 | *5,403,737 | 04/04/95 | Abrahmsen et al. | | | |
| | A2 | *5,629,173 | 05/13/97 | Abrahmsen et al. | | | - 1 |
| | A3 | *5,316,935 | 05/31/94 | Arnold et al. | | | |
| | A4 | *5,208,158 | 05/04/93 | Bech et al. | | | |
| | A5 | *5,244,791 | 09/14/93 | Estell | | | |
| | A6 | *5,316,941 | 05/31/94 | Estell et al. | | | |
| | A7 | *5,955,340 | 02/21/99 | Bott | | | |
| | A8 | *5,340,735 | 08/23/94 | Christianson et al. | | | |

FOREIGN PATENT DOCUMENTS

| EXAM'R INITIAL | | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | Subclass | TRANSLAT'N |
|-------------------|----|--------------------|----------|---------|-------|----------|------------|
| | B1 | EP 0 328 229 A1 | 08/16/89 | EP | | | |
| | B2 | *WO 00/01712 | 01/13/00 | PCT | | | |
| | B3 | WO 91/16423 | 04/18/91 | PCT | | | |
| | B4 | WO 96/27671 | 02/27/96 | PCT | | | |
| | B5 | WO 97/37007 | 10/09/97 | PCT | | | |
| | B6 | WO 98/23732 | 06/04/98 | PCT | | | |
| | B7 | WO 99/20723 | 04/29/99 | PCT | | | |
| | B8 | WO 99/37323 | 07/29/99 | PCT | | | |
| | B9 | WO 99/37324 | 07/29/99 | PCT | - | | |

OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, Etc.)

| C1 | Bech et al., "Chemical Modifications of a Cysteinyl Residue Introduced in the Binding Site of Carboxypeptidase Y by Site-Directed Mutagenesis," <u>Carlsberg Res. Commun.</u> , 53:381-393 (1988) |
|----|---|
| C2 | Bech et al., "Significance of Hydrophobic S ₄ -P ₄ Interactions in Subtilisin 309 from <i>Bacillus Ientus</i> ," Biochemistry, 32:2847-2852 (1993) |
| C3 | Berglund et al., "Altering the Specificity of Subtilisin B. Lentus by Combining Site-Directed Mutagenesis and Chemical Modification," <u>Bioorganic & Mechanical Chemistry Letters</u> , 6:2507-2512 (1996) |
| C4 | *Berglund et al., "Chemical Modification of Cysteine Mutants of Subtilisin <i>Bacillus Lentus</i> Can Create Better Catalysts Than The Wild-Type Enzyme," J. Am. Chem. Soc., 119:5265-5266 (1997) |

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant(s).

| U.S. | DEP | ARTN | 1ENT | OF CO | MME | RCE |
|------|-----|------|------|-------|------|------|
| PA7 | ENT | AND | TRAD | EMAR | K OF | FICE |
| | | | | | | |

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use several sheets if necessary)

| ATTY. | DOCKET | NO. |
|--------|--------|-----|
| GC5/11 | 3.D1 | |

Previously 23623-7076

SERIAL NO.

10/062,970

APPLICANT
Jones et al.

FILING DATE February 1, 2002 GROUP ART UNIT

1623

| | OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, Etc.) |
|-----|---|
| C5 | Betzel et al., "Crystal Structure of the Alkaline Proteinase Savinase TM from <i>Bacillus lentus</i> at 1 4 Å Resolution," <u>J. Mol. Biol.</u> , 223:427-445(1992) |
| C6 | Bonneau et al., "Alteration of the Specificity of Subtilisin BPN' by Site-Directed Mutagenesis in its S ₁ and S ₁ ' Binding Sites," <u>J. Am. Chem. Soc.</u> , 113:1026-30 (1991) |
| C7 | Brocklehurst, "Specific Covalent Modification of Thiols: Applications in the Study of Enzymes and Other Biomolecules," Int. J. Biochem., 10:259-274 (1979) |
| C8 | Bruice et al., "Novel Alkyl Alkanethiolsulfonate Sulfhydryl Reagents. Modification of Derivatives of L-Cysteine," <u>Journal of Protein Chemistry</u> , 1:47-58 (1982) |
| C9 | Chen et al., "Probing the S-1' Subsite Selectivity of an Industrial Alkaline Protease in Anhydrous t-Butanol," <u>Bioorganic & Medicinal Chemistry Letters</u> , 3(4):727-33 (1993) |
| C10 | Davies et al., "A Semisynthetic Metalloenzyme Based on a Protein Cavity That Catalyzes the Enantiosleective Hydrolysis of Ester and Amide Substrates," J. Am. Chem. Soc., 119:11643-11652 (1997) |
| C11 | Davis, B.G., et al., "Altering the specificity of subtilisin Bacillus lentus through the introduction of positive charge at single amino acid sites," <u>Bioorganic and Medicinal Chemistry</u> , (1999 Nov.) 7 (11) 2303-11, XPO000892841 |
| C12 | Davis, B.G., et al., "Controlled site selective protein glycosylation for precise glycan structure catalytic activity relationships," Biorganic & Medicinal Chemistry, Vol. 8, 2000, pp. 1527-1535 |
| C13 | Davis, B.G., et al., "Glycomethanethiosulfonates: powerful reagents for protein glycosylation," Tetrahedron: Asymmetry, NL, Elsevier Science Publishers, Amsterdam, Vol 11, No. 1, January 2000 (2000-01), pp. 245-262 |
| C14 | Davis, B.G., et al., "The controlled introduction of multiple negative charge at single amino acid sites in subtilisin bacillus lentus," <u>Bioorganic and Medicinal Chemistry</u> , (1999 Nov.) 7 (11) 2293-301, XPO000892840 |
| C15 | *Davis, Benjamin G, et al., "Controlled Site Selective Glycosylation of Proteins by a Combined Site Directed Mutagenesis and Chemical Modification Approach," J. Org. Chem., Vol. 63, January 12, 1998 (1998-01-12), pp. 9614-9615 |
| C16 | DeSantis et al., "Chemical Modifications at a Single Site Can Induce Significant Shifts in the pH Profiles of a Serine Protease," J. Am Chem. Soc., 120:8582-8586 (1998) |
| C17 | Desantis, G., et al, "Probing the altered specificity and catalytic properties of mutant subtilisin chemically modified at position S156C and S166C in the S1 pocket," Bioorganic and Medicinal Chemistry, (1997) 7/7 (1381-1387), XP0000892843 |
| C18 | *DeSantis, G., et al., "Site-Directed Mutagenesis Combined with Chemical Modification As a Strategy for Altering the Specificity of the S1 and S1' Pockets of Subtilisin Bacillus Lentus," <i>Biochemistry</i> (1998) 37 (17) 5968-73 |
| C19 | Dickman, M., et al., "Chemically modified mutants of subtilisin bacillus lentus catalyze transesterification reactions better than wild type," <u>Tetrahedron Asymmetry</u> , (11. Dec. 1998) 9/23 4099-4102, XPO000901276. |

EXAMINER DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance *and* not considered. Include copy of this form with next communication to Applicant(s).

U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

URPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)

ATTY. DOCKET NO. GC541-3-D1

Previously 23623-7076

SERIAL NO.

10/062,970

APPLICANT Jones et al. FILING DATE

GROUP ART UNIT 1623

February 1, 2002

| | OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, Etc.) |
|-----|---|
| C20 | Gron et al., "A Highly Active and Oxidation-Resistant Subtilisin-Like Enzyme Produced by a Combination of Site-Directed Mutagenesis and Chemical Modification," <u>Eur. J. Biochem.</u> , 194:897-901 (1990) |
| C21 | Kaiser, "Catalytic Activity of Enzymes Altered at Their Active Sites," Agnew. Chem. Int. Ed. Engl., 27-913-922 (1988) |
| C22 | Kawase et al., "Effect of Chemical Modification of Tyrosine Residues on Activities of Bacterial Lipase," <u>Journal of Fermentation and Bioengineering</u> , 72:317-319 (1991) |
| C23 | Kenyon et al., "Novel Sulfhydryl Reagents," Methods Enzymol., 47:407-430 (1977) |
| C24 | Kluger et al., "Amino Group Reactions of the Sulfhydryl Reagent Methyl Methanesulfonothioate. Inactivation of D-3-hydroxybutyrate Dehydrogenase and Reaction with Amines in Water," Can. J. Biochem., 58:629-632 (1980) |
| C25 | Lloyd, R.C. et al., "Site Selective Glycosilation of Subtilisin Bacillus Lentus Causes Dramatic Increase in Esterase Activity," <u>Biorganic & Medicinal Chemistry</u> , Vol. 8, 2000, pp. 1537-1544 |
| C26 | Lo, Bryan, et al., "Replacement of Ala-166 with Cysteine in the High Affinity Rabbit Sodium Glucose Transporter Alters Transport Kinetics and Allows Methanethiosulfonate Ethylamine to Inhibit Transporter Function," The Journal of Biological Chemistry, 273:2 903-909 (1998) |
| C27 | Neet, K.E. and Koshland, D.E., "The Conversion of Serine at the Active Site of Subtilisin to Cysteine: A 'Chemical Mutation," Proc. Nat. Acad. Sci. USA, 56(5):1606-1611. |
| C28 | Nishimura et al., "Reversible Modification of the Sulfhydryl Groups of Escherichia coli Succinic Thiokinase with Methanethiolating Reagents, 5,5'-Dithio-bis(2-Nitrobenzoic Acid), p-Hydroxymercuribenzoate, and Ethylmercurithiosalicylate," <u>Archives of Biochemistry and Biophysics</u> , 170:461-467 (1975) |
| C29 | Paulson, J.C., "Glycoproteins: what are the sugar chains for?" TIBS, 14:272-276 (1989) |
| C30 | Planas et al., "Reengineering the Catalytic Lysine of Aspartate Aminotransferase by Chemical Elaboration of a Genetically Introduced Cysteine," <u>Biochemistry</u> , 30:8268-8276 (1991) |
| C31 | Plettner, E., et al., "Modulation of Esterase and Amidase Activity of Subtilisin Bacillus Lentus by Chemical Modification of Cysteine Mutants," <u>Journal of the American Chemical Society</u> , (2 Jun. 1999) 121/21, 4977-4981, XPO000891274. |
| C32 | Plettner, Erika et al., "A Combination Approach to Chemical Modification of Subtilisin Bacillus Lentus," <u>Bioorganic & Medicinal Chemistry Letters</u> (Sept. 8, 1998) Vol. 8, No. 17, pp. 2291-2296, XP0004138220 |
| C33 | Polgar et al., "A New Enzyme Containing a Synthetically Formed Active Site. Thiol-Subtilisin," <u>Journal of American Chemical Society</u> , 88:3153-3154 (1966) |
| C34 | Ramachandran et al., "Stabilization of Barstar by Chemical Modification of the Buried Cysteines," <u>Biochemistry</u> , 35:8776-8785 (1996) |
| C35 | Roberts et al., "Reactivity of Small Thiolate Anions and Cysteine-25 in Papain Toward Methyl Methanethiosulfonate," <u>Biochemistry</u> , 25:5595-5601 (1986) |

EXAMINER DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant(s).



U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

STATEMENT BY APPLICANT
(Use several sheets if necessary)

| ATTY. | DOCKET | NO. |
|--------|--------|-----|
| GC541- | 3-D1 | |

Previously 23623-7076

SERIAL NO.

10/062,970

APPLICANT Jones et al.

FILING DATE February 1, 2002 GROUP ART UNIT 1623

OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, Etc.)

| | OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, Etc.) |
|-----|---|
| C36 | Siddiqui et al, "Arthrobacter D-Xylose Isomerase: Chemical Modification of Carboxy Groups and Protein Engineering Of pH Optimum," <u>Biochem. J.</u> , 295:685-691 (1993) |
| C37 | Smith et al., "An Engineered Change in Substrate Specificity of Ribulosebisphosphate Carboxylase/Oxygenase," The Journal of Biological Chemistry, 265:1243-1245 (1990) |
| C38 | Smith et al., "Chemical Modification of Active Site Residues in γ-Glutamyl Transpeptidase," <u>The Journal of Biological Chemistry</u> , 270:12476-12480 (1995) |
| C39 | Smith et al., "Restoration of Activity to Catalytically Deficient Mutants of Ribulosebisphosphate Carboxylase/Oxygenase by Aminoethylation," The Journal of Biological Chemistry, 263:4921-4925 (1988) |
| C40 | Smith et al., "Simple Alkanethiol Groups for Temporary Blocking of Sulfhydryl Groups of Enzymes," <u>Biochemistry</u> , 14:766-771 (1975) |
| C41 | Smith et al., "Subtle Alteration of the Active Site of Ribulose Bisphosphate Carboxylase/Oxygenase by Concerted Site-Directed Mutagenesis and Chemical Modification," <u>Biochemical and Biophysical Research Communications</u> , 152:579-584 (1988) |
| C42 | Spura, A., et al. "Probing Agonist Domain of the Nicotinic Acetylcholine Receptor by Cysteine Scanning Mutogenesis Reveals Residues in Proximity to the Alpha-Bungarotoxin Binding Site, Biochemistry, 20 Apr. 1999 Vol. 38:16 pp. 4912-4921 |
| C43 | Stewart et al., "Catalytic Oxidation of Dithiols by a Semisynthetic Enzyme," J. Am. Chem. Soc., 108:3480-3483 (1986) |
| C44 | Valenzuela et al., "Kinetic Properties of Succinylated and Ethylenediamine-Amidated δ-Chymotrypsins," <u>Biochim. Biophys. Acta</u> , 250:538-548 (1971) |
| C45 | West et al., "Enzymes as Synthetic Catalysts: Mechanistic and Active-Site Considerations of Natural and Modified Chymotrypsin," J. Am. Chem. Soc., 112:5313-5320 (1990) |
| C46 | White et al., "Sequential Site-Directed Mutagenesis and Chemical Modification to Convert the Active Site Arginine 292 Of Aspartate Aminotransferase to Homoarginine," <u>Journal of the American Chemical Society</u> , 114:292-293 (1992) |
| C47 | Wynn et al., "Chemical Modification of Protein Thiols: Formation of Mixed Disulfides," Methods in Enzymology, 251:351-356 (1995) |
| C48 | Wynn et al., "Comparison of Straight Chain and Cyclic Unnatural Amino Acids Embedded in the Core of Staphylococcal Nuclease," Protein Science, 6:1621-1626 (1997) |
| C49 | Wynn et al., "Mobile Unnatural Amino Acid Side Chains in the Core of Staphylococcal Nuclease," <u>Protein Science</u> , 5:1026-1031 (1996) |
| C50 | Wynn et al., "Unnatural Amino Acid Packing Mutants of Escherichia Coli Thioredoxin Produced by Combined Mutagenesis/Chemical Modification Techniques," Protein Science, 2:395-403 (1993) |

15

EXAMINER DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance *and* not considered. Include copy of this form with next communication to Applicant(s).